Corporate Medical Policy: Pegcetacoplan (Empaveli®) **"Notification"** **POLICY EFFECTIVE JANUARY 1, 2026**

Restricted Product(s):

- pegcetacoplan (Empaveli®) subcutaneous infusion for administration by a healthcare professional

FDA Approved Use:

- For the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH)
- For the treatment of adult and pediatric patients aged 12 years and older with C3 glomerulopathy (C3G) or primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN), to reduce proteinuria

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The patient has a confirmed diagnosis of paroxysmal nocturnal hemoglobinuria (PNH) **[medical record documentation required]**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The diagnosis has been confirmed by ALL of the following:
        i. Flow cytometry with at least 2 independent flow cytometry reagents on at least 2 cell lineages (e.g., red blood cells [RBCs] and white blood cells [WBCs]) demonstrating that the patient's peripheral blood cells are deficient in glycosylphosphatidylinositol-anchored proteins (GPI-APs) **[medical record documentation required]**; **AND**
        ii. Laboratory results showing a lactate dehydrogenase (LDH) level ≥ 1.5 times the upper limit of normal at baseline prior to starting complement inhibitor therapy **[medical record documentation required]**; **AND**
        iii. The patient has had at least one PNH-related sign or symptom in the past 3 months prior to starting complement inhibitor therapy (e.g., fatigue, hemoglobinuria, abdominal pain, dyspnea, anemia [hemoglobin < 10 g/dL], history of a major adverse vascular event [including thrombosis], dysphagia, erectile dysfunction, or history of RBC transfusion due to PNH) **[medical record documentation required]**; **AND**
    c. The patient will NOT be using the requested agent in combination with another complement inhibitor used to treat PNH (e.g., crovalimab, an eculizumab product, iptacopan, ravulizumab) **[medical record documentation required]**; **OR**
        i. The patient is transitioning from an eculizumab product to pegcetacoplan therapy **[medical record documentation required]**; **AND**
        ii. The patient will discontinue the eculizumab product 4 weeks after initiation of pegcetacoplan therapy **[medical record documentation required]**; **OR**

2. The patient has a confirmed diagnosis of complement 3 glomerulopathy (C3G) **[medical record documentation required]**; **AND**
    a. The patient is 12 years of age or older; **AND**
    b. The patient has a urine protein-to-creatinine ratio (UPCR) ≥ 0.88 g/g **[medical record documentation required]**; **OR**
        i. The patient has proteinuria greater than 1.0 g/day **[medical record documentation required]**; **AND**
    c. The patient is currently treated with a maximally tolerated renin-angiotensin system (RAS) inhibitor (e.g., angiotensin-converting enzyme inhibitors [ACEi] or angiotensin receptor blockers [ARB]) for at least 90 days **[medical record documentation required]**; **OR**
        i. The patient has a clinical intolerance/contraindication to ALL of the following: angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and combination medications containing an ACEi or an ARB **[medical record documentation required]**; **AND**
    d. The patient has a measured GFR ≥ 30 mL/min/1.73m^2 **[medical record documentation required]**; **AND**
    e. The patient will NOT be using the requested agent in combination with another agent used to treat C3G (e.g., pegcetacoplan, iptacopan) **[medical record documentation required]**; **OR**

3. The patient has a confirmed diagnosis of primary immune-complex membranoproliferative glomerulonephritis (IC-MPGN) **[medical record documentation required]**; **AND**
    a. The patient is 12 years of age or older; **AND**
    b. The patient has a urine protein-to-creatinine ratio (UPCR) ≥ 0.88 g/g **[medical record documentation required]**; **OR**
        i. The patient has proteinuria greater than 1.0 g/day **[medical record documentation required]**; **AND**
    c. The patient is currently treated with a maximally tolerated renin-angiotensin system (RAS) inhibitor (e.g., angiotensin-converting enzyme inhibitors [ACEi] or angiotensin receptor blockers [ARB]) for at least 90 days **[medical record documentation required]**; **OR**
        i. The patient has a clinical intolerance/contraindication to ALL of the following: angiotensin-converting enzyme inhibitors (ACEi), angiotensin receptor blockers (ARB), and combination medications containing an ACEi or an ARB **[medical record documentation required]**; **AND**
    d. The patient has a measured GFR ≥ 30 mL/min/1.73m^2 **[medical record documentation required]**; **AND**
4. The prescriber is a specialist in the area of the patient's diagnosis (e.g., hematologist, oncologist, immunology specialist, nephrologist) or has consulted with a specialist in the area of the patient's diagnosis **[medical record documentation required]**; **AND**
5. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below); **AND**
6. For requests for injection or infusion administration of the requested medication in an **inpatient or outpatient hospital setting**, Site of Care Criteria applies (outlined below)*

Duration of Approval: 90 days (one-time initial approval)***

***NOTE:** This medical policy applies to initial coverage requests only. For continuation of coverage, please submit requests using the member's pharmacy benefit prior authorization submission process. For additional information, please visit the following: https://www.bluecrossnc.com/members/health-plans/forms-resources/drug-search.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
pegcetacoplan (Empaveli®) subcutaneous (SC) infusion	PNH in patients ≥ 18 years old	SC: 1,080 mg infused twice weekly via a commercially available infusion pump	C9399** J3490** J3590**	27,000
	C3G or IC-MPGN in patients ≥ 12 years old, to reduce proteinuria	SC via a commercially available infusion pump: • ≥ 18 years old: 1,080 mg infused twice weekly • 12 years to < 18 years old: ○ ≥ 50 kg: 1,080 mg infused twice weekly ○ 35 kg to < 50 kg: ▪ 1st dose: 648 mg ▪ 2nd dose: 810 mg ▪ Maintenance dose: 810 mg infused twice weekly ○ < 35 kg: ▪ 1st and 2nd dose: 540 mg ▪ Maintenance dose: 648 mg infused twice weekly		

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

***Site of Care Medical Necessity Criteria**

1. For requests for injection or infusion administration in an **inpatient setting**, the injection or infusion may be given if the above medical necessity criteria are met AND the inpatient admission is NOT for the sole purpose of administering the injection or infusion; **OR**
2. For requests for injection or infusion administration in an **outpatient hospital setting**, the injection or infusion may be given if the above medical necessity criteria are met AND ONE of the following must be met:
    a. History of a severe adverse event following the injection or infusion of the requested medication (i.e., anaphylaxis, seizure, thromboembolism, myocardial infarction, renal failure); **OR**
    b. Conditions that cause an increased risk for severe adverse event (i.e., unstable renal function, cardiopulmonary conditions, unstable vascular access); **OR**
    c. History of mild adverse events that have not been successfully managed through mild pre-medication (e.g., diphenhydramine, acetaminophen, steroids, fluids, etc.); **OR**
    d. Inability to physically and cognitively adhere to the treatment schedule and regimen complexity; **OR**
    e. New to therapy, defined as initial injection or infusion OR less than 3 months since initial injection or infusion; **OR**
    f. Re-initiation of therapy, defined as ONE of the following:
        i. First injection or infusion after 6 months of no injections or infusions for drugs with an approved dosing interval less than 6 months duration; **OR**
        ii. First injection or infusion after at least a 1-month gap in therapy outside of the approved dosing interval for drugs requiring every 6 months dosing duration; **OR**
    g. Requirement of a change in the requested restricted product formulation; **AND**
3. If the Site of Care Medical Necessity Criteria in #1 or #2 above are not met, the injection or infusion will be administered in a **home-based infusion** or physician office setting with or without supervision by a certified healthcare professional.

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Hillmen P, Szer J, Weitz I, et al. Pegcetacoplan versus eculizumab in paroxysmal nocturnal hemoglobinuria. *N Engl J Med*. 2021 Mar;384(11):1028-1037.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q2 annually.

January 2026: Criteria change: For PNH indication, added diagnostic criteria requiring flow cytometry and LDH level ≥ 1.5 times the upper limit of normal at baseline prior to starting complement inhibitor therapy. Added age requirement of 12 years or older for C3 glomerulopathy

and primary immune-complex membranoproliferative glomerulonephritis indications according to FDA label. For C3G indication, removed requirement for reduced serum C3. For C3G and IC-MPGN indications, added age requirement according to FDA labeling. **Policy notification given 11/1/2025 for effective date 1/1/2026**.
November 2025: Criteria change: Updated Site of Care medical necessity criteria to add additional bypass for patients with a history of severe adverse events or conditions that cause an increased risk for severe adverse event to align with the Place of Service for Medical Infusions policy for clarity of intent.
August 2025: Criteria change: Added new indication for the treatment of adults and pediatric patients 12 years and older with C3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis, to reduce proteinuria; added associated dosing to FDA label reference table. Updated hemoglobin requirement for paroxysmal nocturnal hemoglobinuria (PNH) indication.
September 2024: Criteria update: Updated list of complement inhibitors not to be used concomitantly to add newly approved crovalimab for clarity.
January 2024: Criteria update: Updated list of complement inhibitors not to be used concomitantly for clarity.
August 2021: Original medical policy criteria issued.